Ventricular arrhythmias in first 12 hours of acute myocardial infarction
Natural history study

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SUMMARY   The prevalence of ventricular arrhythmias in the first 12 hours of acute myocardial infarction has been compared in 17 patients selected on the basis of their developing primary ventricular fibrillation and 21 apparently similar patients without primary ventricular fibrillation. None received or had been receiving antiarrhythmic therapy, digoxin, or diuretics before inclusion in the study. Continuously recorded electrocardiographic tapes were analysed by three independent observers and a specially developed computer system.

The frequency of primary ventricular fibrillation and R-on-T ventricular ectopic complexes was highest in the first three hours after infarction and was lower thereafter. By contrast, other ventricular arrhythmias including ventricular tachycardia increased in frequency in the fourth to twelfth hours. Primary ventricular fibrillation in 16 of the 17 patients was initiated by an R-on-T ventricular ectopic complex $(QR'/QT \leq 0.85)$ while only four of 265 episodes of ventricular tachycardia were so initiated. In the 22 patients (11 with primary ventricular fibrillation, 11 without it) who demonstrated R-on-T ventricular ectopic complexes, the average rate of occurrence of this event was higher in those with primary ventricular fibrillation. In the 10 minutes before primary ventricular fibrillation there was a striking increase in the incidence of R-on-T ventricular ectopic complexes.

This study shows that different ventricular arrhythmias have a different and changing rate of occurrence in acute myocardial infarction. A close relation was observed between R-on-T ventricular ectopic complexes and primary ventricular fibrillation. Though at present this appears not to be of value in predicting primary ventricular fibrillation, it may shed light on the genesis of arrhythmias in infarction and have implications for their prevention.

Ventricular fibrillation is the commonest remediable cause of death in acute myocardial infarction and it is clearly important that it should be predicted and thereby prevented. Soon after the establishment of coronary care units, reports based on observer monitoring of the electrocardiogram suggested that certain types of ventricular arrhythmias preceded ventricular fibrillation and were therefore predictors of it.[1] Subsequently, some ventricular arrhythmias were codified[2] as "warning arrhythmias" and their

detection and treatment became one of the primary roles of the coronary care unit staff.

Three recent reports suggested that these "warning arrhythmias" were as common in patients who did not progress to ventricular fibrillation as in those who did.[3-5] Unlike earlier investigations, these studies had the advantage of continuous recordings of the electrocardiogram. Methodological problems, however, have hampered the description of the natural history of ventricular arrhythmias. In two of these studies[3 5] some patients received antiarrhythmic therapy which would have affected the frequency of the arrhythmias

under investigation. All three studies used Lown's classification[2] in reporting the incidence of "warning arrhythmias" and, therefore, did not consider combinations of specific ventricular arrhythmias, nor the prevalence and change in the prevalence of arrhythmias. In addition the possibility that the significance of ventricular arrhythmias might change with time from the onset of symptoms was not explored.

In order to define the natural history of ventricular arrhythmias in acute myocardial infarction, the electrocardiograms of all patients admitted to a coronary care unit were recorded on magnetic tape. This report is concerned with the incidence and prevalence of ventricular arrhythmias in two selected groups of patients, one of which developed primary ventricular fibrillation and another, apparently comparable group, which did not.

Methods and patients

From February 1977 to May 1979 the electrocardiograms of 1787 patients admitted to the coronary care unit of the Newcastle General and Freeman Hospitals, Newcastle-upon-Tyne, were continuously recorded on magnetic tape. The patients' electrocardiograms were recorded from their admission until discharge from the coronary care unit but only the first 12 hours from the onset of symptoms were analysed for this study. During this time the administration of antiarrhythmic treatment was strictly controlled and was restricted to the following situations: (1) 121 patients receiving antiarrhythmic therapy in a double blind investigation of prophylactic oral tocainide[6]; (2) ventricular tachycardia sustained for more than 30 seconds; (3) ventricular tachycardia of shorter duration causing haemodynamic upset; (4) supraventricular tachycardia or heart block; and (5) ventricular fibrillation.

Patients with acute myocardial infarction who developed ventricular fibrillation in the absence of shock, heart failure, or heart block were considered as having sustained primary ventricular fibrillation.[7] The ventricular fibrillation group was selected from these and consisted of all those patients who had not received any antiarrhythmic therapy (including beta-adrenergic blocking drugs or digitalis) or diuretic therapy in the 72 hours before the onset of symptoms. During the period of investigation, 1066 patients with proven acute myocardial infarction were admitted to the coronary care unit. Forty-nine developed primary ventricular fibrillation, of whom 17 satisfied the stated criteria. Twenty-one comparable patients without primary ventricular fibrillation were identified by the following criteria: (1) all had received placebo therapy in the double blind prophylactic study;[6] (2) all were admitted to the coronary care unit within three hours

of the onset of symptoms; (3) none had received or was receiving any antiarrhythmic therapy (including beta-adrenoreceptor blocking drugs or digitalis) or diuretics in the 72 hours before the onset of symptoms.

The single lead electrocardiogram of all patients was monitored in the coronary care unit in the conventional manner. The electrocardiographic signal and a digitally coded time signal were recorded continuously on reel-to-reel tape recorders. Analysis of the electrocardiograms was performed by three independent observers and by a specially developed computer system based on the Pathfinder analyser and a Digital PDP 11/34 computer.[8]

The Pathfinder was set up to detect all QRS complexes which differed in shape from a previously defined "normal" QRS complex. The electrocardiogram was digitised and samples containing the detected QRS complexes were stored on a computer disc to be recalled for plotting and measurement. These events were considered ventricular ectopic complexes unless clearly preceded by P waves. Electrocardiographic events visually identified by the observers were also stored. The electrocardiograms were analysed in blocks of 10 minutes and all the arrhythmias within each block were documented and all, except single non-R-on-T ventricular ectopic complexes, were printed. Analysis of all patients was from the time of admission to the coronary care unit until 12 hours had elapsed from the onset of symptoms of acute myocardial infarction.

The following definitions of the analysed arrhythmias were employed:

REPETITIVE VENTRICULAR ECTOPIC COMPLEXES
(1) Two consecutive ventricular ectopic complexes (ventricular ectopic pairs): (a) RR interval <500 ms ("fast pair"); (b) RR interval ≥500 ms ("slow pair").
(2) Three or more consecutive ventricular ectopic complexes: (a) ventricular tachycardia – three or more consecutive ventricular ectopic complexes with two successive cycles contained within 1000 ms (equivalent rate ≥120/minute) – this is a conventional definition of ventricular tachycardia; (b) three or more consecutive ventricular ectopic complexes with at least one cycle of ≤500 ms; (c) three or more consecutive ventricular ectopic complexes with no cycle shorter than or equal to 500 ms.

R-ON-T VENTRICULAR ECTOPIC COMPLEXES
R-on-T ventricular ectopic complexes were defined as complexes falling within 85% of the prevailing QT interval of a sinus initiated QRS complex. Single complexes and those that initiated a repetitive ventri-

cular arrhythmia are included. R on ventricular ectopic T waves have not been analysed for this report as the R'−R' interval and QT interval contained in ectopic rhythms are subject to wide interpretative variations.

Results

GROUP CHARACTERISTICS
Table 1 summarises the characteristics of the two study groups with respect to age, sex, smoking history, history of previous infarction, history of previous angina, site of acute myocardial infarction, and the peak serum enzyme level attained. Both groups are comparable in these characteristics apart from a history of previous myocardial infarction which was more common in the patients without ventricular fibrillation.

INITIATION OF VENTRICULAR FIBRILLATION
The initiation of primary ventricular fibrillation in 16 of the 17 patients of the group with ventricular fibrillation was by an R-on-T ventricular ectopic complex. In the remaining patient a brief episode of artefact precluded accurate analysis. All patients were successfully resuscitated.

INCIDENCE OF VENTRICULAR ARRHYTHMIAS
Table 2 illustrates the overall incidence of ventricular arrhythmias in the two study groups. There is a higher patient incidence of repetitive ventricular arrhythmias in the patients without ventricular fibrillation but the patient incidence of R-on-T ventricular ectopic complexes is similar. A total of 69 hours of recorded electrocardiogram was available for analysis of the 17 patients with ventricular fibrillation compared with 216 hours of recorded electrocardiogram analysed for the 21 patients without ventricular fibrillation. An allowance for this disparity of electrocardiographic recording time was made by dividing the patient incidence by the total number of hours of recording. The resultant corrected patient incidence then shows a similar incidence of repetitive ventricular arrhythmias in the two patient groups but a higher incidence of R-on-T ventricular ectopic complexes in the group with ventricular fibrillation.

Five patients with ventricular fibrillation and one patient without ventricular fibrillation had no repetitive ventricular arrhythmias or R-on-T ventricular ectopic complexes during the analysis.

PATTERN OF OCCURRENCE OF VENTRICULAR ARRHYTHMIAS
Fig. 1 depicts the pattern of occurrence of ventricular arrhythmias – primary ventricular fibrillation, R-on-T ventricular ectopic complexes, ventricular tachycardia, pairs of ventricular ectopic complexes, and single ventricular ectopic complexes. In the first three hours after the onset of acute myocardial infarction all these arrhythmias were relatively common. In the fourth to twelfth hours after the onset of acute myocardial infarction the incidence of primary ventricular fibrillation and R-on-T ventricular ectopic complexes was low. The frequency of ventricular tachycardia, pairs of ventricular ectopic complexes, and single ventricular ectopic complexes, however, did not fall and indeed ventricular tachycardia and single ventricular ectopic complex frequency increased in the later hours. The patterns of primary ventricular fibrillation and R-on-T ventricular ectopic complexes were similar and 16 of the 17 episodes of ventricular fibrillation were R-on-T initiated. Ventricular tachycardia in the patients with primary ventricular fibrillation was uncommon, there being only 19 episodes compared with 246 episodes in the 21 patients without ventricular fibrillation. Four runs of ventricular tachycardia were R-on-T initiated (two in one patient with ventricular fibrillation, and one each in two patients without fibrillation. The prevalence of ventricular tachycardia was highest when primary ventricular fibrillation and R-on-T ventricular ectopic complexes were rare.

Table 1 *Characteristics of the two patient groups*

	Patients (n=17) with ventricular fibrillation	Patients (n=21) without ventricular fibrillation
Age (y)	57±7	56±8
Sex	13M 4F	18M 3F
Smokers	13	16
History of previous myocardial infarction	4	8
History of previous angina	8	6
Acute myocardial infarction site		
Anterior	11	11
Inferior	5	10
Posterior	1	0
Peak AST* level (IU/1)	333±208	272±152

* AST, Aspartate transaminase.

Table 2 *Incidence of specific ventricular arrhythmias (see text for arrhythmia definitions)*

	Patient incidence		Corrected patient incidence	
	With ventricular fibrillation (n=17)	Without ventricular fibrillation (n=21)	With ventricular fibrillation (69 h)	Without ventricular fibrillation (216 h)
Repetitive ventricular arrhythmia				
Two complexes (pairs)				
(a) "Fast" pair	9	18	0·13	0·08
(b) "Slow" pair	3	14	0·04	0·06
Three complexes				
(a) Conventional ventricular tachycardia	4	14	0·06	0·06
(b) One R'−R'≤500 ms	4	15	0·06	0·07
(c) All R'−R'>500 ms	3	13	0·04	0·06
R-on-T ventricular ectopic complexes				
One or more	11	11	0·16	0·05
Initiating ventricular arrhythmia	5	4	0·07	0·02
Initiating ventricular tachycardia (definition a)	1	2	0·01	0·01
None of these arrhythmias	5	1	0·07	0·005

RELATION OF R-ON-T VENTRICULAR ECTOPIC
COMPLEXES AND PRIMARY VENTRICULAR
FIBRILLATION

The apparent relation of R-on-T ventricular ectopic
complexes and ventricular fibrillation was
investigated further. The average prevalence of R-on-T ventricular ectopic complexes was calculated for the
patients of the two groups who showed these
arrhythmias (11 with ventricular fibrillation 11
without). Though higher prevalence rates (>1/100
minutes of electrocardiogram) occurred in the
patients with ventricular fibrillation, one patient in
the group without fibrillation showed a high rate and

three of 11 patients with ventricular fibrillation had
rates below this value (Fig. 2).

The temporal relation of R-on-T ventricular ectopic
complexes to ventricular fibrillation was examined by
plotting the incidence of R-on-T ventricular ectopic
complexes during each 10 minute analysis up to, but
not including, the R-on-T ventricular ectopic complex event which initiated ventricular fibrillation (Fig.
3). An increasing number of patients showed R-on-T
ventricular ectopic complexes in the 20 minutes
before ventricular fibrillation. The sharp rise in the
incidence of R-on-T ventricular ectopic complexes
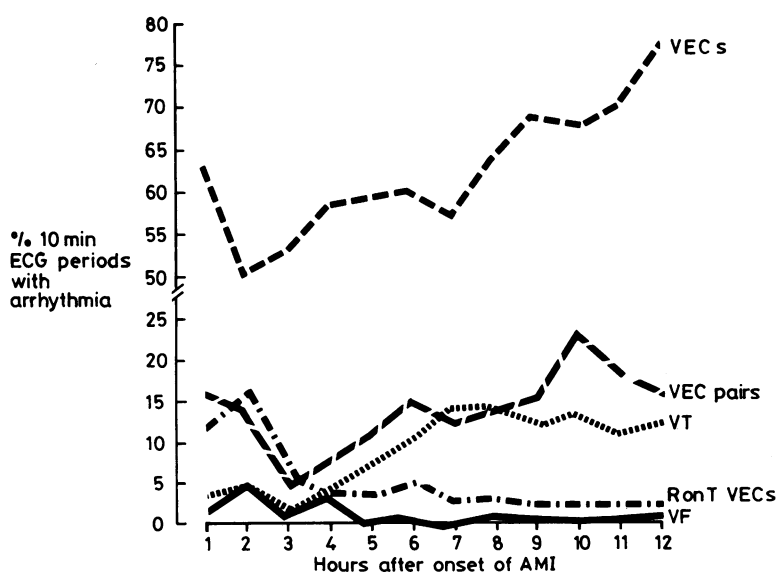cannot be accounted for by variations in the number

Fig. 1 *The percentage of 10 minute electrocardiographic analysis periods containing specific ventricular arrhythmias is shown related to time from the onset of symptoms of acute myocardial infarction*
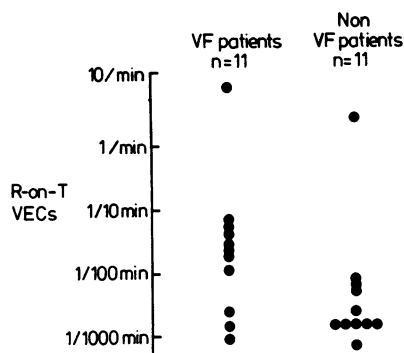
Fig. 2 *The prevalence of R-on-T ventricular ectopic complexes in the 11 patients of each group who showed this arrhythmia.*

of patients under observation. During the last 30 minutes of the analysis the number of patients rose from 13 to 17 but three of the four additional patients had no R-on-T ventricular ectopic complexes and the remaining patient had only a single R-on-T ventricular ectopic complex.

The electrocardiographic records were then examined to ascertain how frequently a change of prevalence of R-on-T ventricular ectopic complexes could be detected in individual patients. A change was defined as either:

(1) A sequential increase of total R-on-T ventricular ectopic complexes in three consecutive 10 minute analysis periods (for example 0–1–2 minimum), or (2) a pronounced increase in total R-on-T ventricular ectopic complexes in two consecutive 10 minute analysis periods (for example 0–2 minimum).

A change, so defined, occurred in 10 patients (six with ventricular fibrillation, four without) from the total of 38 studied. All but one of these patients (a patient without fibrillation) had mean R-on-T ventri-

cular ectopic complex rates >1/100 minutes on the electrocardiogram (Fig. 2). Other definitions of change of R-on-T prevalence were examined but none differentiated the patients with from those without ventricular fibrillation in this analysis.

Discussion

This report is based on data from 38 patients within the early phase of acute myocardial infarction. These patients represent a small portion of the number of patients with proven acute myocardial infarction but we considered it necessary to apply stringent criteria and excluded patients in whom preceding anti-arrhythmic or diuretic therapy might have contributed to the arrhythmia.

Selection of patients for a study of this type is difficult. It is important to exclude patients who have received drugs which may affect the expression of arrhythmias. As the incidence of primary ventricular fibrillation is highest in the early hours after acute myocardial infarction, appropriate patients for comparative analysis with those who develop primary ventricular fibrillation are patients seen as soon as possible after the onset of symptoms. Management of patients after admission to hospital and to the study should be clearly defined and restricted to interventions that are a proven necessity. Analysis of the complex and frequent arrhythmias in the early hours of acute myocardial infarction is demanding and must be meticulous. The system of reporting these arrhythmic events should permit analysis of prevalence and change of prevalence. Critical attention to the timing of events from the onset of symptoms is essential. Few previous studies have satisfied these requirements.

Ventricular arrhythmias of all types have been thought to be most common in the early hours after acute myocardial infarction and to decline with time. While this study can confirm this to be the case for primary ventricular fibrillation and R-on-T ventri-

Fig. 3 *The pattern of occurrence of R-on-T events in the 11 patients with ventricular fibrillation who had R-on-T ventricular ectopic complexes.*
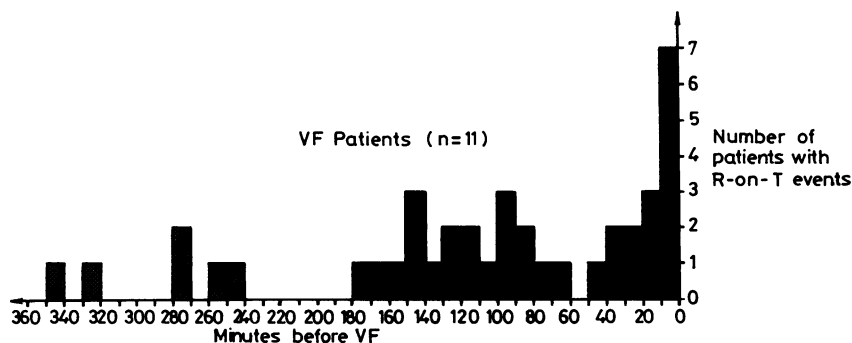
cular ectopic complexes, other ventricular arrhythmias (non R-on-Ts and repetitive ventricular ectopic complexes) may become more common with time in the first 12 hours after infarction. In this study, not only was the pattern of incidence of primary ventricular fibrillation and R-on-T ventricular ectopic complexes similar, but all recorded ventricular fibrillation was initiated by an R-on-T ventricular ectopic complex. El Sherif *et al.*[5] reported the initiation of primary ventricular fibrillation by a non R-on-T ventricular ectopic complex (QR'/QT>1) in seven of 17 patients. In five of these seven, ventricular fibrillation occurred within four hours of the onset of symptoms. Patient selection is a possible explanation of this difference. That study did not exclude patients who had been receiving antiarrhythmic therapy (including beta-adrenoreceptor blocking drugs or digitalis) before admission.

Ventricular tachycardia was rarely initiated by an R-on-T ventricular ectopic complex and its peak occurrence was at a time when R-on-T ventricular ectopic complexes were rare. The finding that ventricular tachycardia is rarely initiated by an R-on-T ventricular ectopic complex accords with reports on clinical[9-12] and experimental[13] infarction.

Many investigators have considered ventricular tachycardia and ventricular fibrillation to be closely related and indeed have referred to ventricular tachycardia and ventricular fibrillation as if they were qualitatively similar. It may be that ventricular fibrillation occurring more than 12 hours after the onset of acute myocardial infarction is more likely to be initiated by degeneration of non R-on-T initiated ventricular tachycardia, but all episodes of ventricular fibrillation in this study occurred within 12 hours of the onset of symptoms and initiation by a ventricular ectopic complex of R-on-T type was a constant finding. This suggests that R-on-T ventricular ectopic complexes were in some way related to this form of primary ventricular fibrillation. In common with other studies using continuous electrocardiographic monitoring, however,[3-5] the crude incidence of R-on-T ventricular ectopic complexes failed to identify those patients who would develop ventricular fibrillation. Though further analysis of the R-on-T ventricular ectopic complexes was applicable to only 11 patients in each of the two groups, there was a notable difference in prevalence and an apparent relation of increasing patient incidence of this phenomenon just before ventricular fibrillation. This finding is clear when the patients are considered as a group, but it is not highly specific in identifying individuals at risk. It may be that a distinct change of prevalence of R-on-T ventricular ectopic complexes would be noticed readily on a conventional coronary care unit monitoring display and so explain the early clinical reports linking R-on-T ventricular ectopic complexes and ventricular fibrillation.

The following observations can be made from this study.
(1) The time dependency of ventricular arrhythmias after acute myocardial infarction differs according to the type of ventricular arrhythmia. Primary ventricular fibrillation and R-on-T ventricular ectopic complexes are an early feature whereas other ventricular arrhythmias have their peak incidence later.
(2) Within the first 12 hours from the onset of symptoms the initiation of primary ventricular fibrillation and ventricular tachycardia is different. Primary ventricular fibrillation is typically R-on-T initiated whereas almost all episodes of ventricular tachycardia are not.
(3) Although the incidence of R-on-T ventricular ectopic complexes in patients is similar in groups with primary ventricular fibrillation and those without, the prevalence of this arrhythmia differs.
(4) A change of the prevalence of R-on-T ventricular ectopic complexes occurs before primary ventricular fibrillation.

The pathogenesis and precursors of ventricular fibrillation may well differ depending on the time after the onset of infarction and the clinical context. The search for precursors of ventricular fibrillation which would be useful in a predictive way has not been successful. There appears to be a relation of R-on-T ventricular ectopic complexes and primary ventricular fibrillation but not between R-on-T ventricular ectopic complexes and ventricular tachycardia nor between ventricular tachycardia and primary ventricular fibrillation. These findings may relate to the different pathogenic mechanisms of arrhythmias at this time in acute myocardial infarction.

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